

# Note on the Jarzynski Equality

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## Abstract

The Jarzynski Equality relates the free energy difference between two equilibrium states of a system to the average of the work over all irreversible paths to go from one state to the other. We claim that the derivation of this equality is flawed, introducing an ad hoc and unjustified weighting factor which handles improperly the heat exchange with a heat bath. Therefore Liphardt et al's experiment cannot be viewed as a confirmation of this equality, although the numerical deviations between the two are small. However, the Jarzynski Equality may well be a useful approximation, e.g. in measurements on single molecules in solution.

## 1 Introduction

Ever since Jarzynski derived a remarkable equality, the Jarzynski Equality<sup>[1,2]</sup>, (JE), his results have been widely used: duplicated theoretically and tested experimentally. It is impossible to do justice to all publications that have appeared in connection with the JE: a survey article would be needed for

that and, in fact, one covering part of the material has been written by Ritort<sup>[3]</sup>. However, in this paper we want to scrutinize the original general derivation of the JE<sup>[1,2]</sup> and discuss briefly a crucial experiment by Liphardt et al<sup>[4]</sup> which was designed to check the JE. The communities accepting the JE consist overwhelmingly of chemists and biophysicists to which also one of us (DM) belongs, while the physicists (to which EGDC belongs) have divided opinions. We hope that this paper may clarify and unify the various aspects of the JE.

The main point of this paper is to argue that the JE is not an equality in any mathematical sense, but can be a useful approximate equality in certain important fields, like, e.g. the study of single molecules in solution.

The JE equates the difference between the free energy of two equilibrium states  $A$  and  $B$  of a system in contact with a heat bath, with an average over the irreversible work done over all paths from  $A$  to  $B$ . This work is done in general by a set of external force centers, which can be characterized by a set of time dependent parameters  $\{\lambda_j(t)\}$  in the Hamiltonian of the system:  $H \equiv H(\{p_i(t)\}, \{q_i(t)\}; \{\lambda_j(t)\}) = H(\Gamma(t); \lambda(t))$ . Here  $\Gamma(t) \equiv \{p_i(t)\}, \{q_i(t)\}$ , defines the microscopic state of the system in its phase space, by giving the values of the momenta  $\{p_i(t)\}$  and coordinates  $\{q_i(t)\}$  respectively, of the  $i = 1, 2, \dots, N$  particles of the system at time  $t$ . For simplicity we will restrict ourselves to only one parameter  $\lambda(t)$ , so that  $j = 1$ . One is interested in the Helmholtz free energy difference  $\Delta F = F_B - F_A$  between the initial and final equilibrium states  $A$  and  $B$ . By considering the work  $W$  done on the system when the external forces bring the system from state  $A$  to state  $B$  along all possible *irreversible* paths, with weights  $e^{-\beta W_{irr}}$ ,

the JE reads:

$$\langle e^{-\beta W_{irr}} \rangle = e^{-\beta \Delta F} \quad (1)$$

where  $\beta = 1/k_B T$ , with  $T$  the temperature of the heat bath and  $k_B$  Boltzmann's constant. Since in (1) the average  $\langle \rangle$  is over the work  $W_{irr}$  done over all possible irreversible paths in phase space from  $A$  to  $B$ , the derivation of the left hand side of Eq.(1) proceeds microscopically via statistical mechanics.

We will consider here the case that the system is for all times  $t \geq 0$  in thermal contact with a heat bath. The heat exchange with the heat bath can be reversible or irreversible, depending on whether it takes place with the internal temperature  $T_I$  of the system equal or not equal to the external temperature  $T_E$  of the heat bath surrounding the system, respectively. In the former case the system will always be in a (canonical) equilibrium state during the work process. As is explained in textbooks of Thermodynamics, a slow or fast work process does not guarantee at all its reversibility or its irreversibility, only the equality of internal and external parameters does.

At  $t = 0$  the system in state  $A$  is coupled to a heat bath of temperature  $T$ , so that its temperature is also  $T$ . It has then a canonical distribution given by<sup>[1]</sup>:

$$f(\Gamma(0), 0) = \frac{1}{Z_0} e^{-\beta H(\Gamma(0), \lambda(0))} \quad (2)$$

Here  $Z_0 = Z_A$  is the canonical partition function at  $t = 0$ , where  $\lambda = \lambda(0) = \lambda_A$ . We assume that work is done on the system during a total time  $\tau$ , so that  $0 \leq t \leq \tau$ , while  $\lambda(t)$  goes from  $\lambda(0) = \lambda_A$  to  $\lambda(\tau) = \lambda_B$ , the final value of  $\lambda$  which corresponds to the equilibrium state  $B$ . The (mechanical) work

$W$  done on the system in an initial micro phase  $\Gamma(0)$  over a time  $t$  will be given by:

$$W_t \equiv W(\Gamma, t) = \int_0^t dt' \frac{\partial H(\Gamma(t'), \lambda(t'))}{\partial \lambda} \dot{\lambda}(t') \quad (3)$$

where  $\dot{\lambda}(t') = d\lambda(t')/dt'$ .

We will assume here for simplicity that the rate of change of  $\lambda$ , i.e.  $\dot{\lambda}$ , is constant.

However, if the change of  $\lambda(t)$  with  $t$  is such that irreversible processes are induced in the system driving it possibly far from equilibrium, then, in order to reach an equilibrium final state  $B$ ,  $\lambda(t)$  must be such that the equilibrium state  $B$  can actually be reached. During this transition, heat exchange will take place (and possibly work will be done). This will depend on the procedure of varying  $\lambda$  with time and on the nature of the induced irreversible processes. The change  $\Delta F$  is computed by Jarzynski considering only the mechanical work in going from  $A$  to  $B$ .

## 2 JE for thermostatted system

Since the system is in constant contact with a heat bath, it becomes important whether the (constant) rate of change  $\dot{\lambda}$  of  $\lambda$  allows thermal equilibrium to be maintained at all times between the system and the heat bath. If it does, the process is reversible<sup>1</sup>, if it does not then the process is irreversible, since the internal and external variables will then not always be

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<sup>1</sup>This is usually formulated by requiring that the external changes induced in the system are slow when compared to the internal relaxation times needed to return to thermal equilibrium once a change of the system (e.g., its volume) has taken place. In that case the temperature of the system and that of the heat bath will always remain the same during a measurement.

equal, or may not even be definable in the system.

In addition, the reversibility can be characterized in a different way, viz., the strength of the coupling of the system to the heat reservoir or the rate of heat transfer, which we will call  $\dot{c}$ . It is this quantity together with the work rate  $\dot{w} = \dot{\lambda} \frac{\partial H}{\partial \lambda}$ , which will determine whether the system will remain in thermal equilibrium at all times i.e., whether a reversible or irreversible process takes place. We can consider now several cases.

- a) The rate of work done on the system  $\dot{w}$  is very small ( $\dot{\lambda} \approx 0$ ) and the coupling  $\dot{c} \approx 0$  also. Then depending on the ratio  $\dot{w}/\dot{c}$ , thermal equilibrium can be maintained between the system and the heat bath, at all times  $0 \leq t \leq \tau$  when  $\dot{w} \ll \dot{c}$ , i.e., there will be plenty of time for the system to exchange heat with the reservoir, so that the disturbance of the system due to the work done on the system and which brings it out of thermal equilibrium, can be readjusted for all  $0 \leq t \leq \tau$  so that the system is always in thermal equilibrium with the heat bath at temperature  $T$ . If this obtains during the entire time  $\tau$  that work is done on the system then the work process is isothermal and reversible.
- b) If the  $\dot{w}$  is very small, but the coupling  $\dot{c}$  is not, then the work process will also be isothermal and reversible.
- c) If, on the other hand,  $\dot{w}$  is very large and the coupling  $\dot{c} \approx 0$ , then there is no way to maintain thermal equilibrium during the work time  $\tau$  and the system is thermodynamically in a non-equilibrium state.
- d) However, if  $\dot{w}$  is very large, then  $\dot{c}$  has to be sufficiently larger to main-

tain thermal equilibrium, if at all possible, and in general one cannot assume that this is so.

### 3 Critique

The above considerations are relevant because, during the evolution of an initial phase  $\Gamma(0)$  of the system, it will not only be subject to the mechanical work done by the external forces via the Hamiltonian  $H$  on the system alone, but also to the simultaneous energy exchange with the heat bath. Therefore, to know the mechanical work and the heat separately along a phase space path, one has, in principle, to know the microscopic state of both the system, the heat bath and their coupling, so as to know whether, and if so, how much and in what direction, heat exchange between the system and the heat bath has taken place.<sup>2</sup>

Consequently the introduction in phase space of the weight  $e^{-\beta W_{irr}}$ , for every irreversible (stochastic) path, where the inverse temperature  $\beta$  of the heat bath is used in the weight for every  $W_{irr}$ , does not seem to make physical sense. In fact, even if the mechanical work  $W_{irr}$  itself could be precisely determined, the canonical weight  $e^{-\beta W_{irr}}$  associated with it, especially when no internal (system) temperature is known or can even be defined - a possibility of being far from equilibrium, which Jarzynski notes himself<sup>[2]</sup> - seems completely arbitrary and the use of the heat bath temperature  $1/\beta$  - the only known temperature available - without foundation. As a consequence,

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<sup>2</sup>For a system in contact with a heat bath the work done on the system is not just the mechanical work, which will change the system's internal energy ( $dE$ ), but also work associated with the heat (energy) exchange with the bath ( $TdS$ ), can already be seen in the isothermal reversible case, where  $dW = dE - dQ = dE - TdS = d(E - TS) = dF$ <sup>[5]</sup>.

an average over the microscopic  $e^{-\beta W_{irr}}$ , as carried out in Eq.(1), does not seem physically meaningful unless they are very close to reversible ones and provide then a good approximation to those. Therefore the JE is correct but trivial if  $W = W_{rev}$  and it seems that the use of  $W_{irr}$  instead of  $W_{rev}$  is, in general, unfounded. A further discussion of this point can be found in points of section 5.

In the above we argued that the heat exchange has not been properly taken into account and an essentially only mechanical theory has been used to derive Eq.(1), while, however, also non-mechanical work e.g. thermal expansion due to heat energy has to be considered.

A striking example of this is Jarzynski's remark<sup>[2]</sup> that it would suffice to let the system evolve from parameter values  $\lambda_A$  to  $\lambda_{B^*} = \lambda_B$  regardless of whether  $B^*$  is the equilibrium state  $B$ , whose free energy difference  $\Delta F$  with state  $A$  one wants. As Jarzynski clearly states, the *non-equilibrium* state  $B^*$  at  $\lambda_{B^*} = \lambda_B$ , reached *before* the equilibrium state  $B$ , can easily be transformed into the desired equilibrium state  $B$ , while the amount of (mechanical) work done to get from  $\lambda_A$  to  $\lambda_B$  remains the same. The only way, however, to go from a non-equilibrium state  $B^*$  with  $\lambda_B$  to an equilibrium state at  $B$ , with no more work done, is through the contact with the heat bath at temperature  $T$ . Since the free energy  $F$  will be a minimum in equilibrium, the non-equilibrium  $\lambda_{B^*} = \lambda_B$  state will, *only if properly chosen*, indeed go to the equilibrium state  $B$ , accompanied, however, with an exchange of an unknown amount of heat and possibly work, which depend on  $B^*$ , all of which will change the free energy.

So far we have discussed the general physical theory of Jarzynski as found

in refs.[1,2]. This theory is supposed to hold for systems of any size. As Jarzynski remarks<sup>[2]</sup> to obtain observable effects the systems have to be small, since otherwise the fluctuations of the work values become too small to be observed. In this connection measurements on single molecules in aqueous solutions seem very appropriate as a check on the JE.

## 4 Experiment

Liphardt et al<sup>[4,6]</sup> have carried out such an experiment on the free energy difference (in their case the Gibbs free energy  $\Delta G$  instead of  $\Delta F$ ) between the unfolded and the folded conformations of a single P5abc RNA molecule, suspended between two handles, in an aqueous salt solution to check the JE. The experiments were carried out carefully, by stretching a single RNA molecule many times, between the folded and unfolded conformations  $A$  and  $B$ . In this case the irreversibility of the procedure manifests itself in hysteresis curves associated with a cycle  $A$  (folded)  $\rightarrow B$  (unfolded)  $\rightarrow A$  (folded). A number of constant stretching (switching) rates of 2 - 5 pN/s (slow) and 34 pN/s and 52 pN/s (fast), (the  $\dot{\lambda}$  above), between folded and unfolded states were applied and histograms were made of the work done versus the extension of the molecule. To obtain statistics, seven independent sets of data were collected for seven different RNA molecules with a slow step between two fast steps and about 40 unfolding-refolding cycles per molecule were performed i.e. about 300 independent measurements were made. Results for the average work differences for these three switching rates relative to the reversible work were plotted in bins of about  $0.7 k_B T$ . Plotting for each switching rate



the most probable value (i.e. the maximum of the Gaussian fits to their histograms) of the work done on each molecule, the fast extension (switching) rates produced work values  $\approx 2 - 3k_B T$ , above the expected thermodynamic free energy difference of about  $60 k_B T$ , because of irreversible contributions (apart from measurement errors) to the work, in agreement with the Second Law of Thermodynamics. On the other hand, an average for each switching rate, using the JE Eq.(1) gave values for the expected free energy difference within their estimated error.

We note that the deviations from equilibrium for even the fastest switching time, are in fact only 5% (or about  $3k_B T$ ), which would not be unusual for such measurements. In addition, the thermal equilibration time is of the order of picoseconds, while we estimate the structural equilibration time to be of the order of milliseconds<sup>[7]</sup> and the experimental switching times of the order of seconds (slow) to 0.1 seconds (fast). Therefore since  $\dot{w} < \dot{c}$ , i.e., essentially reversible isothermal measurements (cases a) and b) above) were performed. Considering the above mentioned time scales, the entire experiment could well be very close to an isothermal one for all switching rates used, so that the JE equality gives results very close to those of using only reversible paths in phase space.<sup>3</sup>

A few additional remarks on this experiment follow.

1. The Liphardt et al. data appear to fit better to the JE for large stretching than to the second cumulant or the “Fluctuation Dissipation Relation (FD)”:

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<sup>3</sup>The remark by Ritort<sup>[3]</sup> that a system may be far from equilibrium even when close to an isothermal process because of its small size does not seem to be correct. The small size will allow the fluctuations to be measurable. However, they have no bearing on the fast change in the control parameter, needed for deviations far from equilibrium.

$\langle W_{irr} \rangle = W_{rev} + \beta\sigma^2/2$ , where  $\sigma^2 = \langle W_{irr}^2 \rangle - \langle W_{irr} \rangle^2$  is the variance of  $W_{irr}$ <sup>4</sup> with  $W_{irr} = W - W_{rev} = W_d$ , the dissipative work. This, in spite of the fact the system is not far from equilibrium.

We note that in the table S1 of the supplementary material their  $\langle W_d \rangle$  (scaled with  $\beta$ ) for various extensions and switching rates are rather close to  $\sigma$ , except  $\langle W_d \rangle$  in the reversible case (very slow switch) where  $\langle W_d \rangle$  is assumed to be zero. If one computes  $\sigma^2/2$ , using the  $\sigma$  in the second column of S1, the resulting  $\langle W_d \rangle$  is too large. If, on the other hand, one corrects the  $\sigma$ 's in the second column for the measurement error by a simple subtraction of the  $\sigma$ 's at  $\langle W_d \rangle = 0$ , the estimates for  $\langle W_d \rangle$  are too small. This bracketing of  $\langle W_d \rangle$  indicates that the data are compatible with  $\langle W_d \rangle = \sigma^2/2$ .

2. We will now derive the JE under three assumptions:

- 1) The  $W_{irr}$  all have the weight  $e^{-\beta W_{irr}}$ , where  $\beta$  is the temperature of the heat bath, not the system;
- 2) a Gaussian assumption is made for the measured non-equilibrium distribution functions;
- 3) a FD of  $\langle W_d \rangle = \frac{\beta\sigma^2}{2}$  has to be used.

Assuming that the distribution functions for  $W_d$  are all Gaussian and using those to fit the data, the left hand side of the JE in eq.(1) can be

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<sup>4</sup>We note that their FD is derived from the JE, thereby assuming its validity, which is supposed to be checked in the experiment. This manifests itself in the appearance of only work contributions to  $\sigma^2$ , while  $\Delta F$  should also contain, in principle, entropic contributions.

written as:

$$\begin{aligned} \langle e^{-\beta W_d} \rangle &= \int d\beta W_d \exp -[\beta W_d - (\beta W_d - \beta^2 \sigma^2 / 2)^2 / 2\sigma^2] \\ &\cdot \left\{ \int d\beta W_d \exp -[\beta W_d - \beta^2 \sigma^2 / 2)^2 / 2\sigma^2] \right\}^{-1} \end{aligned} \quad (4)$$

Carrying out the Gaussian integrals leads then to:

$$\langle e^{-\beta W_d} \rangle = 1 \text{ or } \langle e^{-\beta W_{irr}} \rangle = e^{-\beta W_{rev}} = e^{-\beta \Delta F} \text{ i.e. the JE. This result depends crucially on the validity of } \langle W_d \rangle = \frac{\beta \sigma^2}{2}.$$

We emphasize that two of these three assumptions, although approximately correct, are not justified, as explained above, since the first two are not satisfied in non equilibrium systems.

3. We note that the often quoted claim <sup>[4,11,12]</sup> that the origin of the correctness of the JE is because of the over-weighting of the negative dissipative work balanced by the under weighting the positive dissipative work has no known basis. That the JE works here, in spite of the fact that it is based on unfounded assumptions, is because of a felicitous accident of Gaussian statistics rather than for reasons of thermodynamics and statistical mechanics.

## 5 Discussion

1. As said before, it is clearly impossible to do justice to all the publications that have appeared in connection with the JE. We have confined ourselves here to represent the contents of two articles on the *general foundations* of the JE on Statistical Mechanics by Jarzinski<sup>[1,2]</sup>.

2. In addition we discussed an important experiment which appears to confirm the JE, since the system is in aqueous solution, close to equilibrium and

the processes are (quasi) quasi-static and therefore nearly reversible, in spite of some hysteresis.

3. Although in Liphardts' experiment clear hysteresis loops can be seen, they occur over relatively small parts of the trajectories, which mostly appear to be reversible. True irreversible processes, where e.g. no temperature can be defined in the system, have so far not been considered experimentally (because of the liquid surroundings used so far). Such irreversible processes would question severely the assignments of a canonical weights  $e^{-\beta W_{irr}}$ , with  $\beta$  the temperature of the heat bath.

We note that although to observe the JE the systems have to be small, there is a gap between the experiments performed on biochemical systems (in aqueous solutions) and those on small physical (or chemical) systems without an aqueous heat bath, which have not yet been performed.

4. There are many different theoretical *models*, to mimic the heat bath, which have been used to derive the JE. They are all stochastic and, as far as we are aware, all use Markovian and detailed balance properties, which place them, in our opinion, near predominantly reversible heat exchanges. We confine ourselves again to two examples.

a) This holds for Crooks'<sup>[8]</sup> derivation of the JE for a simple Ising model. He discretizes there the phase space trajectory in sequences of two sub steps, whereby first a control parameter  $\lambda$  does instantaneous work  $W$  on the system followed by an exchange of thermal energy  $E$  with a heat bath. Either the first forward work step is followed by a heat exchange step which lasts sufficiently long compared to the characteristic relaxation times of the system that a state of canonical equilibrium is reached (cf. Crooks' eq.(8)) in which

case the process is a discrete sequence of equilibrium states and therefore a reversible process (like in a reversible experiment) and the JE will be obtained as that for a reversible process. Or the time after the first forward step is not sufficiently long to obtain an equilibrium state, in which case an irreversible process takes place, which may be close to a reversible one, but no detailed balance obtains at any  $\lambda_i$ .<sup>5</sup>

Similarly Jarzynski's procedure applied to the Langevin Equation<sup>[2]</sup>, because of the  $e^{-\beta W_{irr}}$  weight assumption, is restricted to systems near equilibrium, with near reversible heat exchanges.

b) Jarzynski made numerical calculations<sup>[9]</sup> of which we will discuss only that on a harmonic oscillator. He considered  $10^5$  simulations of the work done on a single harmonic oscillator, whose frequency is switched from  $\omega_0 = 1.0$  to  $\omega_1 = 2.0$  over a switching time  $t_s$ . The Hamiltonian of the harmonic oscillator is:

$$H = \frac{p^2}{2} + \omega_\lambda^2 \frac{x^2}{2} \quad (5)$$

where  $\omega_\lambda$  switches from  $\omega_0$  to  $\omega_1 = 2\omega_0$ . If the change from  $\omega_0$  to  $\omega_1$  proceeds infinitely slowly ( $t_s \rightarrow \infty$ ) and adiabatic invariance can be applied, i.e.  $H/\omega = \text{constant}$ , then Jarzynski obtains, for a canonical distribution of initial energies a distribution function for the work  $W$ . Using this to compute the average of the exponential work  $e^{-\beta W}$ , gives  $\beta^{-1} \ln(\omega_1/\omega_0) = 0.693\beta^{-1} = \Delta F$ , since  $\omega_1/\omega_0$  is just the ratio of the canonical partition functions (cf. Jarzynski in ref.9 eq.(59) and fig.3 ( $W^x$  points)). One can get an idea of the average value of  $\beta W$  for fast switchings ( $t_s = 1$ ), by using a similar calculation.

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<sup>5</sup>The assumed detailed balance at every step  $\lambda_i$  is not a direct consequence of microscopic reversibility alone, and has been proved so far only for thermal equilibrium [13,14].

One finds then for the arithmetic average of  $\beta W$  the result  $(\frac{\omega_1}{\omega_0} - 1) = 1$ . Adding then  $W_{rev} = 1$ , a value of 2 is obtained not far from the numerical result (ref.7, fig.3 ( $W^a$ )). However, this result depends critically on the assumption of adiabatic invariance for  $t_s = 1$ , while this actually only holds for  $t_s \rightarrow \infty$ . Moreover, if for example, the energy would change as  $\omega^2$ , the Jarzynski weighting would give  $2\Delta F$  and the arithmetic weighting would give a value 4 instead of 2 for  $\beta W$ .

Jarzynski claims that the JE holds for all systems (not only harmonic oscillators), while we see that the JE is critically dependent on adiabatic invariance for finite  $t_s$ , even for the harmonic oscillator.

5. Finally we note that eq.(1) implies that a remarkable new relation would follow from the  $JE$ , if it were an exact equality, viz.:

$$\langle e^{-\beta W_{irr}} \rangle = \langle e^{-\beta W_{rev}} \rangle \quad (6)$$

In the literature, the eq.(6), or equivalently  $\langle e^{-\beta W_d} \rangle = 1$ , is justified by invoking an apparently very fortuitous general cancellation due to the weighting of  $W_d > 0$  and  $W_d < 0$  with  $e^{-\beta W_d}$ . It is entirely unclear to us, how this can be achieved for irreversible processes in a system, for all  $\lambda(t)$  and all corresponding phase space paths, using in all cases the (unconnected) heat bath temperature  $\beta$  in the weights.

This would imply the equality of the average over the exponentiated work of all irreversible paths from  $A$  to  $B$ , to the (average over all the) reversible path(s) from  $A$  to  $B$ . Considering the unknown nature and wide variety of all irreversible paths this equality does not seem physically understandable. If true, it would incorporate a hitherto unknown symmetry for irreversible

processes for any switching rate, i.e. a new extension of the Second Law. To be sure there are special cases, like those treated in section 4, sub 2 and in section 5, sub 4b, where this equality holds under certain specific assumptions for irreversible processes near equilibrium.

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